

**REMARKS**

Applicants thank Examiner Sisson for his helpful comments conveyed in a telephone interview with Applicants' attorney, Janet M. MacLeod, on January 20 and 21, 2004, for the above-identified application. No exhibits were shown and no demonstrations were conducted during the interview. Claims 23, 24 and 27-46 were discussed. The following prior art was discussed: U.S. Patent Nos. 6,263,095; 6,214,246; 6,174,680; 5,995,650; 5,294,792; and 5,104,621. Agreement was not reached.

In the Office Action mailed September 23, 2003, Claims 23, 24, 27-46 have been rejected under 35 U.S.C. § 103(a) as allegedly rendered obvious by U.S. Patent No. 5,104,621 to Pfoet et al. ("Pfoet et al.") in view of U.S. Patent No. 6,263,095 to Rushbrooke et al. ("Rushbrooke et al.") and U.S. Patent No. 6,214,246 to Craighead ("Craighead"). In the interview on January 20, 2004, the Examiner indicated that Claims 40-45 were not intended to be included in this rejection, since these claims had been previously withdrawn from consideration.

Claims 40-45, directed to non-elected subject matter, have been canceled without prejudice in the interest of advancing prosecution.

In rejecting Claims 23, 24, 27-39 and 46, the Examiner has alleged that Pfoet et al. teach a device comprising a plate for receiving sample receptacles, dispensing means to deliver a sample and/or reagents, illumination means, optical detection means and data storage and analysis means. Rushbrooke et al. allegedly disclose the use of a charge coupled device (CCD) to detect, measure and evaluate light signals resulting from various chemical/biological assays. Craighead allegedly discloses a device comprising an array of reaction sites where simultaneous readouts are obtained for a plurality of reaction sites. The Examiner has alleged that it would have been obvious to modify the device of Pfoet et al. so as to detect, measure and evaluate light signals a plurality of times in a simultaneous manner.

Applicants respectfully submit that the subject matter of Claims 23, 24, 26-39 and 46 is not rendered obvious by the combination of the cited references.

None of the cited references, alone or in combination, teach or suggest an apparatus for simultaneously monitoring an array of reaction sites for light wherein the apparatus comprises a recorder for recording the light intensity level and the time of detection thereof for each of a plurality of liquid samples. Rushbrooke et al. disclose that coordinates from a succession of interrogations of the same sample may be stored in an accumulation store and produced as a list. However, there is no teaching or suggestion in Rushbrooke et al. to record the time at which a particular light emission is recorded.

Further, one would not have been motivated by the cited references to make a device that includes a recorder for recording the light intensity level and time of detection thereof. The device of Pfoest et al. is used to determine optical density of a sample; the device of Rushbrooke et al. is used to detect the presence of a labeled material in a sample; the device of Craighead measures fluorescence of electrophoresed DNA fragments. None of these methods requires determination of variation of light intensity over time, and thus one would not have been motivated to include a means for recording the light intensity level and time of detection thereof. In contrast, the device of the present invention provides a means for recording the light intensity level and time, and thus is useful, for example, in a sequencing by synthesis method as disclosed in the present specification at page 4, lines 12-22.

Claims 23 and 46 have been amended to clarify this aspect of the invention. Support for the amendments may be found in the specification, for example at page 13, lines 9-14 and in Figure 1.

In view of the foregoing comments and amendments, withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

During the telephone interview on January 20 and 21, 2004, the foregoing amendment and remarks were discussed. It is Applicants' understanding that the Examiner indicated that the amendment would be favorably considered subject to a further search of the prior art.

The Examiner subsequently identified U.S. Patent No. 5,294,792 to Lewis et al. ("Lewis et al.") and U.S. Patent No. 5,995,650 to Migdal et al. ("Migdal et al."). The Examiner has alleged that Lewis et al. disclose a device comprising a CCD scanning element in connection

with a processor that records data with a time stamp, at col. 12, line 64 – Col. 13, line 42. The Examiner has alleged that Migdal et al. disclose, at Col. 12, lines 58 – Col. 13, line 15, a device in which a CCD camera is connected to a processor that processes video signals, which arrive as fields or frames of information, and which time stamps the arrival of the fields or frames.

Applicants respectfully submit that Lewis et al. and Migdal et al., cannot be combined with Pfof et al., Rushbrooke et al. and Craighead to provide a *prima facie* case of obviousness because Lewis et al. and Migdal et al. represent non-analogous art. The combination of elements from non-analogous sources, with the benefit of hindsight, cannot support a *prima facie* case of obviousness. In re Oetiker, 997 F.2d 1443, 1447, 24 U.S.P.Q.2d 1443, 1446 (Fed. Cir. 1992). Lewis et al. and Migdal et al. are each non-analogous prior art because these references are neither within the field of the inventors' endeavor nor reasonably pertinent to the problem with which the present inventors were involved, and thereby fail to satisfy the Federal Circuit's two step test for appropriate scope of art. In re Deminski, 796 F.2d 436, 230 U.S.P.Q. 313 (Fed. Cir. 1986).

Lewis et al. disclose a pen computer that acquires data representative of written strokes of the stylus of the pen, recognizes and stores the strokes, and transmits the strokes to a computer. In the pen disclosed by Lewis et al., a mark made by the stylus of the pen is detected by a CCD and may be stored. Lewis et al. disclose that the data may be stored with the time and date of the storing to provide an electronic audit trail, for example to determine the time at which a form was authorized by a signature.

Migdal et al. disclose a computer-aided three dimensional scanning system for measuring and reproducing objects by shape digitizing and adaptive mesh generation. In the computer-aided three dimensional scanning system of Migdal et al., an object is scanned with a geometric light shape such as a laser, the shape of the reflected points of light is recorded by an image collector, and a computer uses the data to reconstruct the three dimensional shape of the object by a triangulation technique. The system comprises a light generator, light positioner, image collector, a frame to orient the foregoing elements, a light source, an audio controller, and a video controller. The video controller accepts and processes video information using a frame

grabber that time stamps arriving fields of frames of information. The frame grabber digitizes the information and sends it to the memory. Programmed elements manipulate the information. The time stamp information is used in a function that synchronizes laser positioning and image processing.

The present invention is directed to an apparatus for monitoring light emitted from an array of reaction sites, for example in a DNA synthesis reaction. Lewis et al. and Migdal et al. are directed to devices completely unrelated to the field of endeavor of the present invention, and thus cannot be used to support a case of obviousness. The cited references cannot be considered analogous art simply because both describe an unrelated apparatus that includes a CCD and a processor.

Further, the cited references are not pertinent to the present inventors' problem of providing a device to monitor an array of reaction sites for light indicating that a reaction is taking place. In the devices of Lewis et al. and Migdal et al., data is recorded with a time stamp for purposes totally unrelated to any aspect of the present invention. The present inventors would not have considered art directed to pens in which data is time stamped to create an electronic audit trail, or computer systems for scanning three dimensional objects in which data is time stamped for use in synchronization software, in achieving the present invention.

Further, the selection of the isolated element of a processor that records the time of data capture, from references directed to completely unrelated devices in which the time stamp performs a completely different function, represents impermissible hindsight reconstruction.

In addition, one of ordinary skill in the art would not have been motivated to combine the cited references. As discussed hereinabove, the device of Pfoest et al. is used to determine optical density of a sample. The device disclosed by Rushbrooke et al. is used to detect the presence of a labeled material in a sample. The device of Craighead is used to measure fluorescence of electroprocessed DNA fragments. None of these devices or methods require a determination of the time at which light is detected, and thus one would not have been motivated to combine these references with an isolated element selected from Lewis et al. or Migdal et al.

In the telephone interview of January 20 and 21, 2004, the Examiner also identified U.S. Patent No. 6,174,680 to Makrigiorgos ("Makrigiorgos"). Makrigiorgos discloses a method for detecting base substitutions using a fluorescent marker molecule, and in which chemiluminescence is detected using a CCD system. At column 24, lines 20-21, Makrigiorgos discloses that the chemiluminescence measurements were performed at least three times. Applicants respectfully submit that Makrigiorgos does not teach that the time of each triplicate measurement is recorded. Further, there would have been no motivation to combine Pfof et al., Rushbrooke et al. and Craighead with Makrigiorgos. As discussed hereinabove, the primary references disclose devices and methods that do not require a determination of light intensity over time, and thus one would not have been motivated to modify such devices to record time.

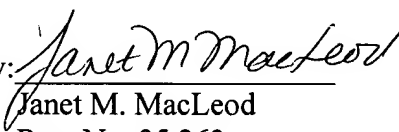
Applicants thank the Examiner for bringing Lewis et al., Migdal et al. and Makrigiorgos to their attention.

In view of the foregoing remarks and amendments, it is respectfully submitted that the present application is in condition for allowance. Entry of the present amendment and favorable consideration of all pending claims is earnestly solicited.

Respectfully submitted,

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